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UROTHELIAL DYSFUNCTION AND CHRONIC INFLAMMATION IN DIABETES MELLITUS PATIENTS WITH OVERACTIVE BLADDER SYNDROME: AN IMMUNOHISTOCHEMISTRY STUDY

Hypothesis / aims of study

Diabetes mellitus (DM) is a metabolic disorder which results from an absolute or relative deficiency of insulin. A number of debilitating urinary symptoms have been reported in patients with DM, namely the diabetic cystopathy/ diabetic bladder dysfunction (DC/ DBD), leading to significant distress and poor quality of life. Although the pathophysiology of DC/ DBD remains unknown, it is suggested that an alteration in detrusor muscle cell physiology, the function of the neuronal component and urothelial dysfunction may play a role. The aim of this study is to investigate the urothelial dysfunction and suburothelial inflammation in DM patients with overactive bladder syndrome (OAB) based on the results of immunohistochemistry study.

Study design, materials and methods

A total of 33 patients with OAB were enrolled in this study. They were subdivided into 2 groups based on the presence of DM or not. Bladder biopsies were performed in 19 patients with OAB and DM, 14 patients with OAB alone and 10 controls. Immunofluorescence staining of junction protein E-cadherin, tryptase for mast cell activation, TUNEL assay for urothelial cell apoptosis, and tight junction protein zonula occluden (ZO-1) were performed. The fluorescence intensity of E-cadherin and ZO-1 was measured using an Image J method. The percentage of apoptotic cells and activated mast cells were measured and quantified as positive cell per area unit (20 μm^2) (Fig.1).

Results

The number of mast cells in the urothelium and suburothelium areas were low in the control group (mean± standard error 1.25 ± 1.15) than that in the OAB groups with or without DM. A highly significant increase in mast cell infiltration was observed in OAB without DM (23.34 ± 7.58, P =0.000) and OAB with DM specimens (19.57 ± 5.04, P =0.000). ZO-1 expression was significantly decrease in OAB without DM (4.49 ± 3.20, P =0.002) and OAB with DM group (5.77 ± 2.89, P =0.003) compared to the control group (11.02 ± 5.66, P=0.000). The E-cadherin expression was also significantly decreased in OAB groups with or without DM (22.16 ± 15.11, P =0.003; 24.89 ± 17.06, P =0.010) compared with the controls (42.4 ± 16.73, P =0.008). TUNEL is the lowest in the control group (0.08 ± 0.26, P =0.011) (Table.1). There was no significant difference in the parameters between OAB patients with and without DM.

Interpretation of results

Defective urothelial barrier function and junction protein and increased suburothelial inflammation and apoptosis are highly prevalent in OAB patients. The results of this study demonstrated that the pathological changes of bladder urothelium were not different between OAB patients with and without DM. The diabetic cystopathy in DM patients might originate from other underlying mechanism other than the urothelial dysfunction.

Concluding message

Urothelial dysfunction and chronic Inflammation may contribute to the pathogeneses of OAB, however, DM does not attribute to the urothelial dysfunction in OAB.

Table .1 Expression of E-cadherin, mast cell, TUNEL and ZO-1 in 3 groups

	Normal (N=10)	OAB patient with DM (N=19)	OAB patient without DM (N=14)	P-value
E-cadherin	42.4 ± 16.7	22.2 ± 15.1	24.9 ± 17.1	0.008
Tryptase (mast cell)	1.25 ± 1.15	23.3 ± 7.58	19.6 ± 5.04	0.000
TUNEL	0.08 ± 0.26	5.21 ± 5.63	5.62 ± 4.71	0.011
ZO-1	11.0 ± 5.66	5.77 ± 2.89	4.49 ± 3.20	0.00

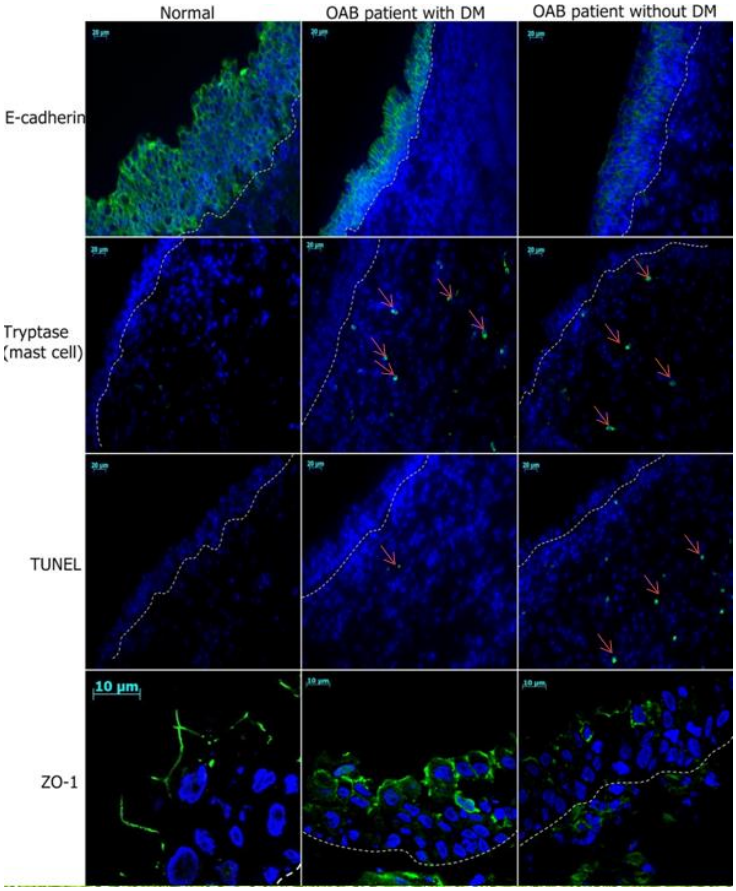

Fig.1. The differences of E-cadherin expression, mast cell count, apoptotic cell count and ZO-1 among the control, OAB with DM and OAB alone. Red arrows represent target cells.

Disclosures
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